US Army Medical Research and Materiel

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Mutants of *Brucella melitensis*

This invention could provide an improved, live-attenuated vaccine to safely and effectively protect against brucellosis in animals. Attenuated, genetically engineered purE gene mutants of *Brucella melitensis* were shown to provide active immunity against infection by *B. melitensis* in mice. The mutants require purines for growth because they lack the purE gene product that is required for the carboxylation of 5'-phosphoribosyl-5-aminoimidazole.

Brucella typically infects domestic and wild animals in the U.S. and people and domestic herds in developing nations. In man, brucellosis may be caused by numerous strains of *Brucella* which also affect cattle, hogs, caribou, sheep, goats, and dogs. The disease is acquired by exposure to infected animals and by ingestion of milk products from such animals. The two current live-attenuated vaccines can only be used in animals as they cause disease in humans. They also cause abortions in adult animals and complicate immunological screening of infected animals.

The invention has numerous potential future applications, including vaccination of animals, dairy workers, animal [illegible], packing house workers, and foreign travelers [illegible] ingest unpasteurized milk. Also, *Brucella* is a biowarfare threat to military personnel, as multiple antibiotic resistant strains of *Brucella* have been constructed. The invention could potentially be used to vaccinate military personnel.

Features and advantages:

- **Attenuated in human monocytes in cell culture, however, capacity to infect is not altered**
- **Attenuated in mice when given orally**
- **Cleared from mouse spleen cells within eight weeks of intraperi-toneal injection**
- **Stimulated protective immunity in mice from intranasal challenge with wildtype *Brucella***
- **Could potentially be combined with other [illegible] improve safety**

Patent Status

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